REMARKS

I. Status of the claims

Applicants' election of the species, "proteins," on March 27, 2002, resulted in examination of claims 1-7 and 9-12 of the present application. Applicants have cancelled claims 3, 4, 5, 10, 11 and 12 without prejudice or disclaimer and reserve the right to pursue examination of those claims in one or more other applications. Applicants added claims 13-20. Accordingly, claims 1, 2, 6-9, 13-20 are currently pending for examination.

Applicants amended claim 1 to delete "cationic polymer" and to instead recite "aminoalkylmethacrylate copolymer or polyvinyl acetal diethylaminoacetate." Support for the recitation of aminoalkylmethacrylate copolymer and polyvinyl acetal diethylaminoacetate can be found at page 4 of the present specification. There, applicants state that "among cationic polymers, a copolymer of aminoalkylmethacrylate or polyvinyl acetal diethylaminoacetate is superior to poly-L-arginine ... in absorption promoting effect." Applicants also teach at page 5 of the specification that "[S]pecific examples of cationic polymers include copolymers of aminoalkylmethacrylate [and] polyvinyl acetal diethylaminoacetate."

Support for a preparation that comprises "0.1 to 90 w/w%" or "1 to 50 w/w%" of aminoalkylmethacrylate copolymer or polyvinyl acetal diethylaminoacetate, as recited in new claims 13 and 14, can be found at page 9. There, applicants state that "[T]he content of a cationic polymer in the powder form preparation of the invention for administration through mucosa is usually 0.1 to 90% (w/w), preferably 1 to 50% (w/w)." Support for the high molecular weight medicines recited in claim 16 can be found at pages 6 and 7 of the specification.

The proteinaceous medicines of high molecular weight recited in claim 16 are supported by applicants' disclosure at pages 6-7 of the specification.

Furthermore, the conjugation of such proteins to haptens or mixture of such proteins with adjuvants is described at page 7 of the specification.

Accordingly, the claimed subject matter is supported and free from objection. Applicants, therefore, respectfully request that the examiner enter and consider the amended and added claims.

II. Summary of the invention

The present invention relates to a preparation, particularly in powder form, that comprises a medicine of high molecular weight and a cationic polymer such as aminoalkylmethacrylate copolymer or polyvinyl acetal diethylaminoacetate, which can be administered to an individual through their mucosa. The latter cationic polymers improve the absorption of the high molecular weight medicines through an individual's mucosa.

III. The Office Action

The examiner rejected the present claims as being either anticipated or rendered obvious by the prior art of record.

IV. Rejection of the claims under 35 U.S.C. § 102(b)

(i) Claims 1, 2, 6, 9 and 10 are not anticipated by WO 93/24149

The examiner states that WO 93/24149 "discloses a powder composition containing HPMC, chitosan, and a medicament," and that the reference teaches "application to mucosa."

Applicants respectfully disagree and traverse the rejection. The composition of WO 93/24149 discloses a pharmaceutical composition which comprises non-ionic cellulose ether derivative (including hydroxypropylmethyl cellulose) and a chitin-derived polymer (*e.g.*, chitosan). The cellulose and the chitosan are added for improved adhesiveness on the nasal mucosa and sustained release of the active ingredient. WO 93/24149 does not teach that this composition is formulated so that the absorption of the active ingredient

(*i.e.*, the "medicament") through the mucosa is accelerated. Furthermore, neither aminoalkylmethacrylate copolymer nor polyvinyl acetal diethylaminoacetate, both cationic polymers, are described in WO 93/24149, and the reference does not suggest or hint that such cationic polymers may be formulated with the prescribed medicament.

(ii) Claims 1, 7, 9, 10 and 11 are not anticipated by JP 07-118170

The examiner states that JP 07-118170 "discloses a powdery composition for nasal administration containing chitosan and an active peptide." However, JP 07-118170 does not teach or suggest combining aminoalkylmethacrylate copolymer or polyvinyl acetal diethylaminoacetate to a medicine of high molecular weight, as is presently claimed. Accordingly, the present claims are not anticipated by JP 07-118170.

V. Rejection of the claims under 35 U.S.C. § 103(a)

(i) Claim 5 is not unpatentable over WO 93/24149 or JP 07-118170 in view of JP 10-095738

The examiner states that neither WO 93/24149 nor JP 07-118170 teaches a composition containing polyarginine, but that JP-10-095738 teaches a transmucosal preparation containing a medicament and poly-L-arginine. The examiner further asserts that "the arginine compound raises the permeation rate of the medicament transmucosally, increasing its therapeutic effect." Thus, the examiner alleges that "it would have been obvious ... to combine the references since all the references teach a method of improving transmucosal absorption of a medicament." The examiner concludes that "one would be motivated to use polyarginine in a mucosal composition" such as that described in WO 93/24149 or JP 07-118170.

Applicants disagree. The present claim recites subject matter directed to a powder form of a preparation for administration through mucosa, wherein the powdered preparation specifically comprises either aminoalkylmethacrylate

copolymer or polyvinyl acetal diethylaminoacetate. No combination of the cited prior art references teaches or suggests the formulation of a composition with either cationic polymer nor a composition that further comprises a high molecular weight medicine and also polyarginine. Accordingly, the originally-filed claim 5 is not obvious over the cited prior art. Nevertheless, since applicants have now cancelled claim 5, the examiner's rejection is moot.

(ii) Claim 4 is not unpatentable over WO 93/24149 or JP 07-118170 in view of JP 4026617

The examiner admits that neither WO 93/24149 or JP 07-118170 teaches "the instant cationic polymer (AEA)," but that JP 4026617 teaches an agent matrix containing an active agent and AEA ("polyvinyl acetal diethylamino acetate") for nasal mucosa. The examiner concludes that "one would be motivated to use JP 4026617's cationic polymer AEA with a reasonable expectation of obtaining similar results since WO 93/24149 and JP 07-118170 both teach cationic polymers and active agent composition for mucosa."

Applicants disagree and traverse the rejection. JP 4026617 discloses a nose drop in which polyvinyl acetal diethylamino acetate (AEA) is combined to an active ingredient so as to improve the residency of the drug in the nasal cavity. Furthermore, the use of AEA facilitates the local delivery of the active ingredient to a specific part of the nose, *i.e.*, to the nasal mucosa. This is contrary to the present invention wherein applicants' preparation acts systemically when applied through the nasal mucosa. Thus, none of the cited prior art references teach or suggest the use of a cationic polymer, such as aminoalkylmethacrylate copolymer or polyvinyl acetal diethylaminoacetate, for systemic administration of the presently claimed powder preparation. Nevertheless, since applicants have now cancelled claim 4, the examiner's rejection is moot.

(iii) Claims 1-7 and 9-12 are not unpatentable over WO 90/09780

The examiner contends that WO 90/09780 discloses an active agent and a polycationic substance for administration to mucosa and teaches that that inventive composition can be in powder or microsphere form. However, the examiner admits that the reference "does not specify the preparation in powder form in the examples or exemplify the instant cationic polymers." Furthermore, WO 90/09780 teaches neither a powdered preparation containing a high molecular weight medicine nor one of the specific cationic polymers recited in amended claim 1. To this end, the present application discloses that the claimed cationic polymers, aminoalkylmethacrylate copolymer or polyvinyl acetal diethylaminoacetate are effective in improving absorption of high molecular weight medicines through mucosa than are other polycationic substances, such as chitosan and DEAE-dextran, the two substances described in WO 90/09780. Accordingly, applicants respectfully request that the examiner withdraw this rejection.

In view of the foregoing amendments and remarks, applicants respectfully request favorable reconsideration and allowance of the pending claims. If there are any issues remaining which the examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the examiner is hereby respectfully invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

Date: 12 August 2003

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MARKED-UP VERSION OF THE CLAIMS

1. (Once amended) A preparation in powder form for administration through mucosa, comprising a medicine of high molecule weight and [a cationic polymer] aminoalkylmethacrylate copolymer or polyvinyl acetal diethylaminoacetate.

8. (Once amended) The preparation of claim 7, wherein the [bioactive peptide] protein is a granulocyte colony-stimulating factor.

9. (Once amended) The preparation of any one of claims 1, 2, 6, 7, or 13-20, which is a preparation for pernasal administration.